Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 2 of 38

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A compound of formula

$$(R^{1})_{m} \xrightarrow{X-Y} (CH_{2})_{q} \xrightarrow{R^{4}} R^{6} \xrightarrow{R^{7}} O \xrightarrow{R^{3}} (R^{9})_{t}$$

wherein

m is 0, 1, 2, 3 or 4;

 $\label{eq:continuous} \mbox{each R^1 independently represents halogen, cyano, hydroxyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy or sulphonamido;}$

either X represents a bond, -CH₂-, -O- or -C(O)- and Y represents a bond, -CH₂-, -O- or -C(O)-, or X and Y together represent a group -CH=C(CH₃)- or -C(CH₃)=CH-, and Z represents a bond, -O-, -NH- or -CH₂-, provided that only one of X, Y and Z can represent a bond at any one time and provided that X and Y do not both simultaneously represent -O- or -C(O)-;

n is 0, 1 or 2; each R^2 independently represents halogen or C_1 - C_6 alkyl; q is 0 or 1; R^3 represents -NHC(O) R^{10} ; -C(O) $NR^{11}R^{12}$ or -COOR^{12a};

Attorney's Docket No.: 06275-427US1 / 100684-1P US

Applicant : Hossain et al. Serial No.: 10/520,699 Filed : January 7, 2005

Page : 3 of 38

 R^4 . R^5 . R^6 . R^7 and R^8 each independently represent a hydrogen atom or a C_1 - C_6 alkyl group;

t is 0, 1 or 2:

each R 9 independently represents halogen, cyano, hydroxyl, carboxyl, C1-C6 alkoxy, C1-C6 alkoxycarbonyl, C1-C6 haloalkyl, or C1-C6 alkyl optionally substituted by at least one substituent selected from carboxyl and C1-C6 alkoxycarbonyl;

R + -represents a group C1-C6-alkvl. C2-C6-alkenyl, C3-C6-eyeloalkyl, adamantyl, C5-C6 eycloalkenyl, phenyl or a saturated or unsaturated 5- to 10 membered heterocyclic ring system comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, each of which may be optionally substituted by one or more substituents independently selected from nitro, hydroxyl, oxo, halogen, earboxyl, C1-C6-alkyl, C1-C6-alkoxy, C1-C6-alkylthio, C₁-C₆-alkylearbonyl, C₁-C₆-alkoxycarbonyl, phenyl and NHC(O) R - or R represents a group NR 14 R 15 or O-R 16;

 R^{11} and R^{12} each independently represent (i) a hydrogen atom, (ii) a 3- to 6-membered saturated or unsaturated ring optionally comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur and optionally further comprising a bridging group, the ring being optionally substituted with at least one substituent selected from halogen, hydroxyl, C1-C6 alkyl, C1-C6 hydroxyalkyl and C1-C6 haloalkyl,

- (iii) a C1-C6 alkyl group optionally substituted by at least one substituent selected from halogen, amino, hydroxyl, C1-C6 haloalkyl, carboxyl, C1-C6 alkoxy, C1-C6 alkoxycarbonyl, C1-C6 alkylcarbonylamino and a 3- to 6-membered saturated or unsaturated ring optionally comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur and optionally further comprising a bridging group, the ring being optionally substituted with at least one substituent selected from halogen, hydroxyl, oxo (=O), C1-C6 alkyl, C1-C6 hydroxyalkyl and C1-C6 haloalkyl, or (iv) C1-C6 alkylsulphonyl, or
- R 11 and R 12 together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring that optionally further comprises a ring nitrogen, oxygen or sulphur

Applicant: Hossain et al. Serial No.: 10/520,699 Filed: January 7, 2005

Page : 4 of 38

atom and that is optionally fused to a benzene ring to form a 8- to 11-membered ring system, the heterocyclic ring or ring system being optionally substituted with at least one substituent selected from halogen, hydroxyl, amido, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxycarbonyl, C₁-C₆ haloalkyl, C₁-C₆ alkylamino, di-C₁-C₆ alkylamino, C₁-C₆ alkylamino, C₁-C₆ alkylaminocarbonyl, C₁-C₆ alkylaminocarbonyl, phenyl, phenylcarbonyl, phenylcarbonyloxy and hydroxydijphenylmethyl;

 $\ensuremath{\text{R}}^{12a}$ represents a hydrogen atom or a $C_1\text{-}C_6$ alkyl group;

R¹³-represents a C₁-C₆-alkyl, amino or phenyl group;

R¹⁴ and R¹⁵ each independently represent a hydrogen atom, or a group C₁-C₆ alkyl, C₁-C₆ alkylsulphonyl, phenyl or a saturated or unsaturated 5 to 10 membered heterocyclic ring system comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, each group being optionally substituted as defined above for R¹⁰ or

R¹⁴ and R¹⁵ together with the nitrogen atom to which they are attached form a 4-to 7-membered saturated heterocyclic ring that optionally further comprises a ring nitrogen, oxygen or sulphur atom, the heterocyclic ring being optionally substituted by at least one hydroxyl; and R¹⁶ represents a hydrogen atom, or a group C₁-C₆ alkyl, phenyl or a saturated or unsaturated 5-to 10-membered heterocyclic ring system comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, each group-being optionally substituted as defined above for R¹⁰;

or a pharmaceutically acceptable salt thereof.

(Currently amended) A compound according to claim 1, wherein
m is 0, 1, 2, 3 or 4;
each R¹ independently represents halogen, cyano, hydroxyl, C₁-C₆ alkyl,

C1-C6 alkoxy or sulphonamido;

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 5 of 38

either X represents a bond, -CH₂-, -O- or -C(O)- and Y represents a bond, -CH₂-, -O- or -C(O)-, or X and Y together represent a group -CH=C(CH₃)- or -C(CH₃)=CH-, and Z represents a bond, -O-, -NH- or -CH₂-, provided that only one of X, Y and Z can represent a bond at any one time and provided that X and Y do not both simultaneously represent -O- or -C(O)-;

n is 0, 1 or 2; each R^2 independently represents halogen or $C_1\text{-}C_6$ alkyl; q is 0 or 1; $R^3 \text{ represents } \xrightarrow{\text{-NHG(O)}R}^{10}_{\text{-F}} \text{-C(O)}\text{NR}^{11}R^{12} \text{ or -COOR}^{12a};$ $R^4, R^5, R^6, R^7 \text{ and } R^8 \text{ each independently represent a hydrogen atom or a } C_1\text{-}C_6 \text{ alkyl}$

t is 0, 1 or 2;

group;

each R^9 independently represents halogen, cyano, hydroxyl, C_1 - C_6 alkoxy, C_1 - C_6 haloalkyl, or C_1 - C_6 alkyl optionally substituted by at least one substituent selected from carboxyl and C_1 - C_6 alkoxycarbonyl;

R¹⁰ represents a group C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₆-cycloalkyl, adamantyl, C₅-C₆-cycloalkenyl, phenyl or a saturated or unsaturated 5- to 10-membered heterocyclic ring system comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, each of which may be optionally substituted by one or more substituents independently selected from nitro, hydroxyl, oxo, halogen, carboxyl, C₁-C₆-alkyl, C₁-C₆-alkoxy, C₁-C₆-alkylthio; C₁-C₆-alkylcarbonyl, C₁-C₆-alkoxycarbonyl, phenyl and NHC(O). R¹³, or

R 10 represents a group NR 14 R 15 or O R 16;

R¹¹ and R¹² each independently represent (i) a hydrogen atom, (ii) a 3- to 6-membered saturated or unsaturated ring optionally comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, the ring being optionally substituted with at least one substituent selected from halogen, methyl and trifluoromethyl, or

(iii) a C_1 - C_6 alkyl group optionally substituted by at least one substituent selected from halogen,

Applicant: Hossain et al. Serial No.: 10/520,699 Filed: January 7, 2005 Page: 6 of 38

amino, hydroxyl, trifluoromethyl, carboxyl, C_1 - C_6 alkoxycarbonyl and a 3- to 6-membered saturated or unsaturated ring optionally comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, the ring being optionally substituted with at least one substituent selected from halogen, methyl and trifluoromethyl, or

 R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring optionally further comprising a ring oxygen atom, the heterocyclic ring being optionally substituted with at least one substituent selected from hydroxyl and C_1 - C_6 alkoxy;

R^{12a} represents a hydrogen atom or a C₁-C₆ alkyl group;

R¹³ represents a C₁-C₆-alkyl, amino or phenyl group;

R¹⁴ and R¹⁵ together with the nitrogen atom to which they are attached form a 4- to 7membered saturated heteroevele: and

R¹⁶ represents a hydrogen atom, or a group C₁-C₆ alkyl, phenyl or a saturated or unsaturated 5 to 10 membered heterocyclic ring system comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, each group being optionally substituted as defined above for R¹⁰;

or a pharmaceutically acceptable salt $\underline{\text{thereof}}$.

 (Previously presented) A compound according to claim 1, wherein X and Y have the meanings shown in the following table: Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 7 of 38

X	Y
bond	0
0	bond
CH ₂	bond
bond	CH ₂
CH ₂	0
0	CH ₂
C(O)	0
0	C(O)
CH ₂	CH ₂
-CH=C(CH ₃)-	

- (Previously presented) A compound according to claim 1, wherein Z represents a bond,
 or -CH₂-.
- 5. (Currently amended) A compound according to claim 1, wherein R^3 represents $-NHC(O)R^{10}$ or $-C(O)NR^{11}R^{12}$.
- 6. (Previously presented) A compound according to claim 1, wherein t is 0, 1 or 2.
- 7. (Previously presented) A compound according to claim 1, wherein each R^9 independently represents halogen, hydroxyl, carboxyl, C_1 - C_4 alkoxy, C_1 - C_4 alkoxycarbonyl, C_1 - C_4 haloalkyl or C_1 - C_4 alkyl.
- (Currently amended) A compound according to claim 1 selected from:

 N-(2-{((2S) 3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxyl-phenyl)acetamide,

 N-(2-{((2S) 3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropylloxyl-4-fluorophenyl)acetamide.

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 8 of 38

N-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropylloxyl-4 methoxyphenyl)acetamide.

N (2 [[(2S) 3 (5 Chloro 1'H,3H spiro[1-benzofuran-2,4' piperidin] 1' yl) 2-hydroxypropylloxyl 4-hydroxyphenyllacetamide.

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-N-cyclopropylbenzamide,

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-N-cyclopropyl-4-fluorobenzamide,

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-N-cyclopropyl-4-methoxybenzamide,

 $N - (2 - \{ [(2S) - 3 - (5 - Chloro - 1'H, 3H \cdot spiro[1 - benzofuran - 2, 4' - piperidin] - 1' \cdot yl) - 2 \cdot hydroxy - 2 \cdot methylpropyl]oxy] - 4 \cdot hydroxyphenyl)acetamide trifluoroacetate,$

N (5-Chloro 2-{[(2S) 3-(6-chloro-1'H,3H-spiro[2-benzefuran-1,4' piperidin]-1'-yl)-2-hydroxypropyl]oxy}phenyl)acetamide,

N (2 [[(2S) 3 (6 Chloro 1'H,3H-spiro[2-benzofuran-1,4' piperidin] 1' yl) 2-hydroxypropyl]oxyl 4 fluorophenyl)acetamide;

N·(2 [[(28) 3-(6-Chloro-1²H,3H-spiro[2-benzofuran-1,4²-piperidin]-1²-yl)-2-hydroxypropyl]oxy]-4-methoxyphenyl)acetamide;

2-{[(2S)-3-(6-Chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-N-cyclopropyl-4-fluorobenzamide,

N-(2{[(28)-3 (5-Fluoro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]phenyl)acetamide,

Applicant: Hossain et al. Serial No.: 10/520,699 : January 7, 2005 Filed

Page : 9 of 38

N (4 Chloro 2 [[(2S) 2 hydroxy 3 (3 oxo 1'H,3H spiro[2 benzofuran 1,4' piperidin]-1'-yl)propylloxy) phenyl)acetamide,

N-Cyclopropyl-2-{[(2S)-2-hydroxy-3-(1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'vl)propylloxy}benzamide,

N-(4-Chloro 2-[[(2S) 2-hydroxy 3-(1'H,3H-spiro[2-benzofuran 1,4' piperidin] 1'yl)propylloxylphenyl)acetamide,

N (5 Chloro 2 (((28) 2 hydroxy 3 (1'H3H spiro[2 benzofuran 1.4' piperidin] 1' vl)propylloxy) phenyl)acetamide,

N (2-[[(2S) 2-hydroxy-2-methyl-3-(1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1' vl)propylloxy) -4-methoxyphenyl)acetamide.

N [2 ([(2S) 2 Hydroxy 3 (1'H,3H spiro[2 benzofuran 1,4' piperidin]-1' yl)propylloxy)-5-(trifluoromethyl)phenyllacetamide,

N (2-(f(2S) 2-Hydroxy-3-(2-methyl-1'H-spirofindene-1.4' piperidin] 1'vl)propylloxy) phenyl)acetamide.

N (2-{[(2S) 3-(2,3-Dihydro-1'H-spiro[indene-1,4'-piperidin]-1'-yl)-2hydroxypropylloxy) phenyl)acetamide.

N (2 ([(2S) 2 Hydroxy 3 (2 oxo 1'H spiro[1 benzofuran 3.4' piperidin] 1' yl)propylloxy) phenyl)acetamide,

2-{[(2S)-3-(5-Chloro-1'H.3H-spiro[1-benzofuran-2.4'-piperidin]-1'-v])-2hydroxypropylloxy\-N-cyclopropyl-4-hydroxybenzamide,

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxy-2methylpropylloxy}-N-cyclopropyl-4-hydroxybenzamide.

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-vl)-2-hydroxy-2methylpropyl]oxy}-4-hydroxy-N-methylbenzamide (trifluoroacetate),

2-{[(2S)-3-(5-Chloro-1'H.3H-spiro[1-benzofuran-2.4'-piperidin]-1'-vl)-2-hydroxyloxy}-4hydroxy-N-methylbenzamide,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 10 of 38

N (2-{[(2S) 3 (5 Chloro 1'H spiro[1,3 benzodioxole 2,4' piperidin] 1' yl) 2 hydroxy 2-

hydroxypropylloxy)-4-hydroxyphenyl)acetamide trifluoroacetate.

methylpropyl]oxy] 4 hydroxyphenyl)acetamide trifluoroacetate,

N (4 Hydroxy 2 ff(25) 2 hydroxy 3 (1 H spirof 1.3 benzodioxole 2.4 pineridin) 1.

A' (4 Hydroxy 2 [[(25) 2 hydroxy 3 (1'M-spiro[1,3-benzodioxole-2,4' piperidin] 1'yl)propyl]oxyl phenyl)acetamide trifluoroacetate,

N-(4-Hydroxy-2-{[(2S) 2-hydroxy-2-methyl-3 (1¹H-spiro[1,3-benzodioxole-2,4'-piperidin]-1'-yl)propyl]oxy)phenyl)acetamide trifluoroacetate;

N (2 [[(28) 3 (5 Chloro 1'H,3H-spiro[2-benzofuran-1,4' piperidin] 1' yl) 2-hydroxypropylloxyl 4 hydroxyphenyl)acetamide.

- N (2 - ([(2S) 3 (5 - Chloro 1'H,3H spiro[2-benzofuran 1,4'-piperidin] 1'-yl) 2-hydroxypropy[]oxy]phenyl)acetamide,

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-N-methylbenzamide,

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxy-2-methoxypropyl]oxy}-N-cyclopropyl-4-hydroxybenzamide,

 $2-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-hydroxy-N-(2-hydroxyethyl)benzamide,$

 $\label{eq:N-2-Aminoethyl} $$N-(2-Aminoethyl)-2-{(](2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzamide,$

2-{[(2S)-3-(5-Fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hvdroxypropylloxy}-4-hydroxy-N-methylbenzamide.

nydroxypropyrjoxy;-4-nydroxy-14-metnyloenzamide,

N-(2-[[(28) 3-(5-Fluoro-1'H,3H-spiro[1-benzofuran-2,4' piperidin]-1'-yl)-2-hvdroxypropylloxyl-4-hydroxyphenyllacetamide.

N (2 ([(28) 3 (5 Fluoro 1'H,3H-spiro[1-benzofuran 2,4' piperidin] 1' yl) 2-hydroxypropy[]oxy]phenyl)acetamide;

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 11 of 38

N-[2-({(2S) 3-{(2S) 5-Chloro-1'H,3H-spiro[1-benzofuran-2,3'-pyrrolidin]-1'-yl]-2-hvdroxypropylloxylphenyllacetamide.

N [2 ({(2S) 3[(2R) 5 Chloro 1'H,3H-spiro[1-benzofuran 2,3'-pyrrolidin] 1'-yl] 2-hydroxypropyl)oxy)phenyllacetamide,

N[2 (((2S) 3 [(2R) 5 Chloro 1'H,3H spiro[1-benzofuran 2,3'-pyrrolidin] 1'-yl] 2-hydroxypropyl|oxy) 4 methoxyphenyl|acetamide,

2-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[1-benzofuran-2,3'-pyrrolidin]-1'-yl)-2-hydroxypropylloxy}-4-hydroxy-*N*-methylbenzamide,

2-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropylloxy}-4-hydroxybenzoic acid (trifluoroacetate).

3(S)-1-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzoyl)pyrrolidin-3-ol,

3(R)-1-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzoyl)pyrrolidin-3-ol,

3-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-(morpholin-4-ylcarbonyl)phenol, and pharmaceutically acceptable salts of any one thereof.

9. (Currently amended) A compound according to claim 1 selected from:

N·(2-{[(28) 3 (5-Chloro 1'H,3H-spiro[1-benzofuran-2,4' piperidin] 1'-yl) 2-hydroxypropyl]oxy]phenyl)acetamide,

N·(2-{[((28) 3 (5-Chloro 1'H,3H-spiro[1-benzofuran-2,4' piperidin] 1'-yl) 2-hydroxypropyl]oxy] 4-fluorophenyl)acetamide,

N·(2-{[((28) 3 (5-Chloro 1'H,3H-spiro[1-benzofuran-2,4' piperidin] 1'-yl) 2-hydroxypropyl]oxy] 4-methoxyphenyl)acetamide.

Applicant: Hossain et al. Serial No.: 10/520,699 Filed: January 7, 2005 Page: 12 of 38

N·(2 [[(2S) 3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4' piperidin] 1'-yl) 2-hydroxypropyl]oxy]. 4-hydroxyphenyl)acetamide;

N [2 [[(2S) 3 (5 Chloro-1'H,3H-spiro[1-benzofuran 2,4' piperidin] 1' yl) 2-hvdroxvpropylloxy) -5 (trifluoromethyl)phenyllacetamide.

2-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropylloxyl-N-cyclopropylbenzamide.

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-N-cyclopropyl-4-fluorobenzamide,

2-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-N-cyclopropyl-4-methoxybenzamide,

N (2 [[(2S) 3 (5 Chloro 1'H,3H spiro[1 benzofuran 2,4' piperidin] 1' yl) 2 hydroxy 2-methylpropylloxyl 4 hydroxyphenyl)acetamide trifluoroacetate.

N (5-Chloro-2-[[(2S)-3-(6-ehloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy]phonyl)acetamide,

N (2 [[(28) 3 (6 Chloro 1'H,3H spiro[2 benzofuran 1,4' piperidin] 1' yl) 2-hydroxypropylloxyl 4 fluorophenyl)acetamide,

N·(2-[[(2S) 3-(6-Chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxyl-phenyl)acetamide,

2-{[(2S)-3-(6-Chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-N-cyclopropyl-4-fluorobenzamide,

 $N-(2\{\{(28)-3-(5-Fluoro-1^2H,3H-spiro[2-benzofuran-1,4^2-piperidin]-1^2-yl)-2-hydroxypropyl]phenyl)acetamide,$

N (4 Chloro 2 [[(28) 2-hydroxy-3 (3-oxo-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)propyl]oxy}phenyl)acetamide,

Applicant : Hossain et al. Serial No. : 10/520,699 Filed : January 7, 2005 Page : 13 of 38

N-Cyclopropyl-2-{[(2S)-2-hydroxy-3-(1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)propyl]oxy}benzamide,

N (4-Chloro 2 [[(2S) 2 hydroxy 3 (1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)propylloxylphenyl)acetamide.

N (5 Chloro 2 [[(28) 2 hydroxy 3 (1'H,3H-spiro[2-benzofuran-1,4' piperidin] 1'-yl)propylloxyl-phenyllacetamide.

N [2 - [[(28) 2 Hydroxy 3 (1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)propyl]oxyl - 5 - (trifluoromethyl)phenyl]acetamide.

N (2 - [[(28) 2 Hydroxy 3 (2-methyl-1'H-spiro[indene-1,4'-piperidin]-1'-y\)propyl]exy\phenyl)acetamide,

 $\label{eq:N-2-2} N \ (2 - \{\{(2S) \ 2 - Hydroxy - 3 - (2 - oxo - 1'H \cdot spiro[1 - benzofuran - 3,4' \cdot piperidin] - 1' - y!\}propy!]oxy] phenyl)acetamide,$

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-N-cyclopropyl-4-hydroxybenzamide,

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxy-2-methylpropyl]oxy}-N-cyclopropyl-4-hydroxybenzamide,

 $\label{eq:N-def} $$N_{4-\text{hydroxy-2-}([(2S)-2-\text{hydroxy-3-}(1'H,4H-\text{spiro}[\text{chromene-3,4'-piperidin}]-1'-\text{yl})propyl-phenyl)acetamide,}$

 $2-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxy-2-methylpropyl]oxy\}-4-hydroxy-N-methylbenzamide (trifluoroacetate),$

 $2-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxy]oxy\}-4-hydroxy-N-methylbenzamide, \\$

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 14 of 38

N (2-{[(2S) 3 (5-Chloro-1'H spiro[1,3-benzodioxole 2,4' piperidin]-1'-yl)-2-

hydroxypropylloxy) 4-hydroxyphenyl)acetamide trifluoroacetate,

N (2 - [[(2S) 3 (5 Chloro 1'H-spiro[1,3-benzodioxole 2,4' piperidin] 1' yl) 2-hydroxy-2-methylpropylloxy) 4-hydroxyphenyllacetamide trifluoroacetate.

N-(4 Hydroxy 2-[[(28) 2-hydroxy 3-(1'H-spiro[1,3-benzodioxole-2,4'-piperidin]-1'yl)propylloxyl phenyl)acetamide trifluoroacetate,

N-(4 Hydroxy 2-[[(25) 2-hydroxy 2-methyl 3-(1'H-spiro[1,3-benzodioxole-2,4'-piperidin]-1'-yl)propyl]oxy} phenyl)acetamide trifluoroacetate;

N (2 {[(2S) 3 (5 Chloro 1'H,3H-spiro[2-benzofuran 1,4'-piperidin] 1'-yl) 2-

hydroxypropyl]oxy} 4 hydroxyphenyl)acetamide,

N (2 [[(2S) 3 (5 Chloro 1'H,3H-spiro[2-benzofuran 1,4' piperidin] 1' yl) 2-hydroxypropylloxyl phenyl)acetamide,

2-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropylloxy}-4-hydroxy-*N*-methylbenzamide.

 $2-\{[(2S)-3-(5-Chloro-1^{1}H_{3}H-spiro[2-benzofuran-1,4^{2}-piperidin]-1^{2}-yl)-2-hydroxy-2-methoxypropyl]oxy\}-N-cyclopropyl-4-hydroxybenzamide,$

2-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-*N*-(2-hydroxyethyl)benzamide,

 $\label{eq:N-2-Aminoethyl} $$N-(2-Aminoethyl)-2-{||(2S)-3-(5-chloro-1)^2H}_3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-hydroxybenzamide,$

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxyethyl)benzamide,

N (2 [[(28) 3 (5 Fluoro 1'H,3H-spiro[1 benzofuran 2,4' piperidin] 1'-yl) 2hydroxypropyl]oxy] 4 hydroxyphenyl)acetamide, N (2 [[(28) 3 (5 Fluoro 1'H,3H-spiro[1 benzofuran 2,4' piperidin] 1'-yl) 2-

hydroxypropyl]oxy}phenyl)acetamide,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 15 of 38

N-[2-(!(2S)-3[(2S)-5-Chloro-1'H,3H-spiro[1-benzofuran 2,3' pyrrolidin]-1'-yl]-2-hydroxypropyl}oxy)phenyllacetamide,

N-[2 (((2S) 3 [(2S) 5 Chloro 1'H,3H-spiro[1-benzofuran 2,3' pyrrolidin] 1'-yl] 2-hvdroxypropylloxy) 4 methoxyphenyllacetamide.

N [2 (!((2S) 3 [(2R) 5 Chloro 1'H,3H-spiro[1-benzofuran 2,3'-pyrrolidin] 1'-yl] 2-hydroxypropylloxy) 4 methoxyphenyllacetamide.

2-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[1-benzofuran-2,3'-pyrrolidin]-1'-yl)-2-hydroxypropylloxy}-4-hydroxy-*N*-methylbenzamide,

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzoic acid (trifluoroacetate),

 $\label{eq:condition} 3(S)-1-\{2-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-hydroxybenzoyl)pyrrolidin-3-ol,$

 $\label{eq:condition} 3(R)-1-(2-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-hydroxybenzoyl)pyrrolidin-3-ol,$

 $3-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-(morpholin-4-ylcarbonyl)phenol,$

2-{[(2S)-3-(5-chloro-1'H-spiro[1,3-benzodioxole-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-N-methylbenzamide trifluoroacetate,

N (2 - [[(2S) 3 - (6-chloro -3,4-dihydro -1 H-spiro[ehromene -2,4' piperidin] -1' yl) 2hydroxypropyl]oxy} phenyl)acetamide trifluoroacetate;

N (2 [[(28) 3 (6 chloro 3,4 dihydro 1'H spiro[chromene 2,4' piperidin] 1' yl) 2hydroxypropyl]oxy] 4 fluorophenyl)acetamide trifluoroacetate,

2-{[(2S)-3-(6-chloro-3,4-dihydro-1'H-spiro[chromene-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-N-methylbenzamide trifluoroacetate,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 16 of 38

 $\label{eq:N-2-likelihood} $$ N (2-\{\{(2S) -3 -(6-\text{chloro} -3,4-\text{dihydro} -1 - H-\text{spiro} \{\text{chromene} -2,4'-\text{piperidin}\} -1'-yl) -2-\text{hydroxypropyl} = N-\text{ydroxypheny} = N-\text{ydroxy$

N (2 {[(2S) 3 (6 chloro 3,4 dihydro 1'H-spiro[chromene 2,4' piperidin] 1' yl) 2

hydroxy-2-methylpropyl]oxy}-4-hydroxyphenyl)acetamide trifluoroacetate,

N [2 (((2S) 3 [(2R) 5 chloro 1''H,3H-spiro[1 benzofuran 2,3' pyrrolidin] 1'-yl] 2-hydroxypropylloxy) 4 hydroxyphenyllacetamide.

N[2 (((28) 3 [(28) 5 chloro 1''H,3H-spiro[1-benzofuran 2,3'-pyrrolidin] 1'-yl]-2-hydroxypropyl}oxy) 4-hydroxyphenyl]acetamide,

3-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropylloxy}-4-(pyrrolidin-1-ylcarbonyl)phenol,

1-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzoyl)piperidin-4-ol,

(3S)-1-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}benzoyl)pyrrolidin-3-ol,

 $3-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-(piperidin-1-ylcarbonyl)phenol,$

 $(3S)-1-\{2-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-hydroxybenzoyl)pyrrolidin-3-ol,$

 $1-(2-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-hydroxybenzoyl)piperidin-4-ol,$

N [4-Hydroxy-2-(((2S)-2-hydroxy-3-[5-(trifluoromethyl)-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl]propyl]oxy)phenyl]acetamide,

(3S)-1-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-hydroxybenzoyl)pyrrolidin-3-ylbenzoate,

(3S)-1-(2-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-fluorobenzoyl)pyrrolidin-3-ol,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 17 of 38

(3S)-1-[4-Hydroxy-2-({(2S)-2-hydroxy-3-[5-(trifluoromethyl)-1'H,3H-spiro[1-benzofuran-2.4'-piperidin]-1'-vllpropyl}oxy)benzovllpyrrolidin-3-ol.

(3S)-1-(4-Fluoro-2-{[(2S)-2-hydroxy-3-(1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-y|)propylloxy|benzoy|)pyrrolidin-3-ol,

4-Fluoro-2-{[(2S)-3-(5-fluoro-1'*H*,3*H*-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropylloxy}benzoic acid (hvdrochloride).

(3S)-1-(4-Fluoro-2-{[(2S)-3-(5-fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}benzoyl)pyrrolidin-3-ol,

 $\label{eq:N-[(2S)-1-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzoyl)pyrrolidin-3-yl]acetamide,$

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-methylbenzoic acid hydrochloride,

 $(3S)-1-(2-\{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy]\}-4-methylbenzoyl)pyrrolidin-3-ol,$

2-{[(2S)-3-(5-Fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-methylbenzoic acid hydrochloride,

 $(2S)-1-(5-Chloro-1^2H_3H-spiro[1-benzofuran-2,4^2-piperidin]-1^2-yl)-3-(2-\{[2-(hydroxymethyl)morpholin-4-yl]-arbonyl\}-5-methylphenoxy)propan-2-ol,$

 $(3S)-1-(2-\{[(2S)-3-(5-Fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-methylbenzoyl)pyrrolidin-3-ol,$

2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropy]oxy}-N-{[(4R)-2.5-dioxoimidazolidin-4-yl]methyl}-4-hvdroxybenzamide,

 $1-(2-\{[(2S)-3-(5-Chloro-1)^2H, 3H-spiro[1-benzofuran-2,4)^2-piperidin]-1, -yl)-2-(2-f[(2S)-3-(5-Chloro-1)^2H, 3H-spiro[1-benzofuran-2,4)^2-piperidin]-1, -yl)-2-(2-f[(2S)-2-(5-Chloro-1)^2H, 3H-spiro[1-benzofuran-2,4)^2-piperidin$

 $hydroxypropyl] oxy\}-4-hydroxybenzoyl)-3-(trifluoromethyl) pyrrolidin-3-ol,\\$

3-{[(2S)-3-(5-Chloro-1'*H*,3*H*-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-{[3-(trifluoromethyl)pyrrolidin-1-yl]carbonyl} phenol, Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 18 of 38

N-[2-(Acetylamino)ethyl]-2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzamide,

N (5-chloro 2-[[(2S)-3-(5-chloro 1'H₃H-spiro[1-benzofuran 2,4'-piperidin] 1'-yl) 2hydroxypropylloxy] 4-methoxyphenyl)acetamide.

(3S) N (5-chloro-2-{[(2S) 3-(5-chloro-1/H,3H-spire[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropylloxylphenyl)-3-hvdroxypropylloxylphenyl)-3-hvdroxypropylloxylphenyl)-3-hvdroxypropylloxylphenyl)-3-hvdroxypropylloxylphenyl

(3S) N (2- [[(2S)-3 (5-chloro 1'H;3H spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}phenyl)-3-hydroxypyrrolidine-1-carboxamide,

N (2 {[(2S) 3 (5 chloro 1'H,3H-spiro[1 benzofuran 2,4'-piperidin] 1' yl) 2

hydroxypropyl]oxy) phenyl) 4 hydroxypiperidine 1 carboxamide,

N (2-[[(28) 3-(5-Chloro 1'H,3H-spiro[1-benzofuran 2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy]phonyl)urea-trifluoroacetate,

N (2 [[(28) 3 (5-chloro 1'H₃H spiro[1-benzofuran 2,4' piperidin] 1'-yl) 2-hydroxypropyl]oxy] 4-hydroxyphenyl)urea trifluoroacetate,

N'(2-[[(2S)-3 (5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropy|loxy|-4-fluorophenyl)urea trifluoroacetate.

N [[(2 * [[(2S) 3 (5 Chlore -1'H,3H spire[1 benzofuran 2,4'-piperidin] -1'-yi) 2hydroxypropyl]oxy] -4 hydroxyphenyl)amino]carbonyl}methanesulfonamide trifluoroacetate,

(4S)-2-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzoyl)isoxazolidin-4-ol trifluoroacetate,

(4R)-2-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-hydroxybenzoyl)isoxazolidin-4-ol trifluoroacetate,

(4S)-2-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-hydroxybenzoyl)-4-methylisoxazolidin-4-ol trifluoroacetate,

(4R)-2-(2-{[(2S)-3-(5-Chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropylloxy}-4-hvdroxybenzoyl)-4-methylisoxazolidin-4-ol trifluoroacetate.

Applicant : Hossain et al. Serial No. : 10/520,699 Filed : January 7, 2005 Page : 19 of 38

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropylloxy}-N-(methylsulfonyl)benzamide trifluoroacetate,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hvdroxypropylloxy}-N-1H-tetrazol-5-ylbenzamide bis(trifluoroacetate).

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenol bis(trifluoroacetate).

 $3-\{[(2S)-3-(5-\text{chloro-}1'H,3H-\text{spiro}[1-\text{benzofuran-}2,4'-\text{piperidin}]-1'-yl)-2-\\ \text{hydroxypropyl]oxy}-4-\{[(3S)-3-(\text{dimethylamino})\text{pyrrolidin-}1-yl]\text{carbonyl}\}\\ \text{phenol bis(trifluoroacetate)},$

(3S)-1-(5-chloro-2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzoyl)pyrrolidin-3-ol trifluoroacetate,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hvdroxypropyl]oxy}-4-{[(3S)-3-methoxypyrrolidin-1-yl]carbonyl}phenol trifluoroacetate,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-{[(2R)-2-(hydroxymethyl)pyrrolidin-1-yl]carbonyl}phenol trifluoroacetate.

3-{[(2S)-3-(5-chloro-1/H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-{[(2S)-2-(hydroxymethyl)pyrrolidin-1-yl]carbonyl}phenol trifluoroacetate.

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-{[3-(hydroxymethyl)pyrrolidin-1-yl]carbonyl}phenol trifluoroacetate,

1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxybenzoyl)-D-prolinamide trifluoroacetate,

 $\label{eq:N-4-hydroxy-3-(1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-y+)propy-]-phony-y-benzofuran-2,4'-piperidin-1'-y+)propy-y-phony-y-benzofuran-2,4'-piperidin-1'-y-y-propy-y-phony-y-ph$

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 20 of 38

N-(4-hydroxy-2-{[(2S)-2-hydroxy-3-(5-methyl-l-H,3H-spiro[1-benzofuran-2,4'-piperidin]-l'-yl)propyl]oxyl phenyl)acetamide trifluoroacetate,

N (5-chlore 2- [[(2S) 2-hydroxy-3 (1'H,3H-spire[1-benzofuran 2,4'-piperidin]-1'yl)propyl]oxy] 4-methoxyphenyl)acetamide trifluoreacetate;

N (5-chloro 4-hydroxy-2-{[(2S) 2-hydroxy-3 (1'H,3H-spiro[1-benzofuran 2,4'-piperidin] 1'-yhpropylloxyl phenyllacetamide trifluoroacetate.

peridinj-1-yi)propyrjoxy) pnenytjacetamide trifiuoroacetate,

(38) N·(2-[[(28) 3 (5-chloro-17H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy]. 4-methoxyphenyl) 3-hydroxypyrrolidine-1-carboxamide-trifluoroacetate.

(3S) N (2 {[(2S) 3 (5-chloro 1'H,3H-spiro[1-benzofuran 2,4'-piperidin] 1'-yl) 2-

hydroxypropyl]oxy]-4-hydroxyphenyl)-3-hydroxypyrrolidine-1-carboxamide trifluoroacetate,

(3S)-1-(4-hydroxy-2-{[(2S)-2-hydroxy-3-(1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)propyl]oxy}benzoyl)pyrrolidin-3-ol trifluoroacetate,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-5-methylbenzoic acid hydrochloride,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropyl]oxy}-4-methoxybenzoic acid hydrochloride.

 $(3S)-1-\{2-\{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-5-methylbenzoyl)pyrrolidin-3-ol trifluoroacetate,$

 $(3S)-1-(2-\{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-methoxybenzoyl)pyrrolidin-3-ol trifluoroacetate,$

5-chloro-2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy} benzoic acid hydrochloride,

 $(3S)-1-(5-chloro-2-\{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\} benzoyl) pyrrolidin-3-ol trifluoroacetate,$

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-5-fluorobenzoic acid hydrochloride,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 21 of 38

(3S)-1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-5-fluorobenzoyl)pyrrolidin-3-ol trifluoroacetate,

N (2-[[(2S) 3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}phenyl)pyrrolidine-1-carboxamide trifluoroacetate,

Methyl 4 (acetylamino) 3 - [[(2S) 3 (5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl) 2-hydroxypropylloxyl benzoate trifluoroacetate.

4 (acetylamino) 3 ([(2S) 3 (5-chloro 1'H,3H-spiro[1-benzofuran 2,4'-piperidin] 1'-yl) 2-hydroxypropylloxylbenzoio acid trifluoroacetate.

N-(2-{{(2S)-3-(5-ehloro-3'-fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropylloxyl-4-hvdroxyphenyllacetamide.

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxypropyl)benzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl] oxy \} - 4 - hydroxy - N - (2 - hydroxy - 1, 1 - dimethylethyl) benzamide, \\$

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-N-cyclopentyl-4-hydroxybenzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-N-(2-methoxyethyl)benzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxyphenyl)benzamide,

N-(tert-butyl)-2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxvpropvlloxv}-4-hvdroxvbenzamide.

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxy-1-methylethyl)benzamide,

2-{{(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-N-isobutylbenzamide,

Applicant : Hossain et al. Serial No. : 10/520,699 Filed : January 7, 2005 Page : 22 of 38

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N-(4-hydroxycyclohexyl)benzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-N-(2,3-dihydroxypropyl)-4-hydroxybenzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxyethyl)-N-methylbenzamide,

Methyl N-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-hydroxybenzoyl)serinate,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

 $\label{lem:hydroxypropyl} $$ hydroxypropyl] oxy}-N-(1-ethylpropyl)-4-hydroxybenzamide,$

hydroxypropyl]oxy}-4-hydroxy-N-(tetrahydrofuran-2-ylmethyl)benzamide,

 $hydroxypropyl] oxy\}-4-hydroxy-N-[1-(hydroxymethyl)-2,2-dimethylpropyl] benzamide,\\$

 $\label{lem:hydroxypropyloxy} $$-N-{[(1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]methyl}-4-hydroxybenzamide,$

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl] oxy\}-4-hydroxy-N-[1-(hydroxymethyl)-2-methylpropyl] benzamide,\\$

 $hydroxypropyl] oxy\}-4-\{[4-(2-hydroxyethyl)piperazin-1-yl]carbonyl\}phenol,\\$

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-{[3-(hydroxymethyl)piperidin-1-yl]carbonyl}phenol,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-N-[5-(1,1-dimethylpropyl)-2-hydroxyphenyl]-4-hydroxybenzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N-[3-(1-hydroxyethyl)phenyl]benzamide,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 23 of 38

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-N-(cyclopropylmethyl)-4-hydroxybenzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N-pyrrolidin-1-ylbenzamide,

N-[(1R,4S)-bicyclo[2.2.1]hept-2-yl]-2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-

2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzamide,

4-(4-chlorophenyl)-1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzoyl)piperidin-4-ol,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-v])-2-

hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxy-1-phenylethyl)benzamide,

1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxybenzoyl)-4-phenylpiperidin-4-ol,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-(3,4-dihydroisoquinolin-2(1H)-ylcarbonyl)phenol,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl] oxy\}-4-\{[2-(hydroxymethyl)piperidin-1-yl]carbonyl\}phenol,\\$

 $1-(2-\{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,5'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,5'-piperidin]-1'-yl)-2-(2-f((2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,5'-piperidin]-1'-yl)-$

 $hydroxypropyl] oxy \}-4-hydroxybenzoyl)-N, N-dimethylprolinamide,\\$

Methyl (4R)-1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

(3R)-1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxybenzoyl)piperidin-3-ol,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxycyclohexyl)benzamide,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-[(4-phenylpiperidin-1-yl)carbonyl]phenol,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 24 of 38

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-(thiomorpholin-4-ylcarbonyl)phenol,

1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxybenzoyl)piperidin-3-ol,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-N-(cyclopropylmethyl)-4-hydroxy-N-propylbenzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N,N-diisobutylbenzamide,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl] oxy \}-4-(1,3-dihydro-2H-isoindol-2-ylcarbonyl) phenol,\\$

N-(2-tert-butoxyethyl)-2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-N-isobutylbenzamide,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-[(4-fluoropiperidin-1-yl)carbonyl]phenol,

 $3-\{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-(2S)-3-(2S)-$

 $hydroxypropyl] oxy \}-4-[(4,4-difluor opiperid in-1-yl) carbonyl] phenol,\\$

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-N-phenylbenzamide,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl] oxy\} - 4 - (\{(2R)-2-[hydroxy(diphenyl)methyl]pyrrolidin-1-yl\} carbonyl) phenol, \\$

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl] oxy\}-4-hydroxy-N-(2-hydroxyethyl)-N-methylbenzamide,\\$

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-(pyrrolidin-1-ylcarbonyl)phenol,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-{[4-(2-hydroxyethyl)piperazin-1-yl]carbonyl}phenol,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 25 of 38

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-vl)-2-

hydroxypropyl]oxy}-4-{[3-(hydroxymethyl)piperidin-1-yl]carbonyl}phenol,

4-(4-chlorophenyl)-1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-vl)-2-hvdroxvpropvl]oxv}-4-hvdroxvbenzovl)piperidin-4-ol.

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-{[4-(hydroxymethyl)piperidin-1-yl]carbonyl}phenol,

1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxybenzoyl)-4-phenylpiperidin-4-ol,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl] oxy \} -4 - (3,4 - dihydroisoquinolin -2 (1 H) - ylcarbonyl) phenol, \\$

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-{[2-(hydroxymethyl)piperidin-1-yl]carbonyl}phenol,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl] oxy\}-4-\{[3-(dimethylamino)pyrrolidin-1-yl]carbonyl\}phenol,\\$

 $1-(2-\{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-henzofuran-1,4'-piperidin]-1'-yl)-1'-yl$

 $hydroxypropyl] oxy\}-4-hydroxybenzoyl)-\textit{N,N}-dimethylprolinamide,}$

 $hydroxypropyl] oxy\}-N-cyclohexyl-4-hydroxy-N-(2-hydroxyethyl) benzamide,\\$

Methyl (4R)-1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hvdroxypropyl]oxy}-4-hydroxybenzoyl)-4-hydroxyprolinate.

(3R)-1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hvdroxvpropylloxy}-4-hvdroxvbenzovl)piperidin-3-ol.

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-vl)-2-

hydroxypropyl]oxy}-4-[(4-phenylpiperidin-1-yl)carbonyl]phenol,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-(thiomorpholin-4-ylcarbonyl)phenol,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 26 of 38

1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropylloxy}-4-hydroxybenzoyl)piperidin-3-ol.

nydroxypropyrjoxy;---nydroxyochzoyr)piperidin-5-oi,

 $2-\{[(2S)-3-(5-\text{chloro-1'}H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl)-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl\}$

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl]oxy\}-N-(cyclopropylmethyl)-4-hydroxy-N-propylbenzamide,\\$

hydroxypropylloxy}-4-hydroxy-N.N-diisobutylbenzamide.

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-v])-2-

hydroxypropyl]oxy}-4-(1,3-dihydro-2H-isoindol-2-ylcarbonyl)phenol,

N-(2-tert-butoxyethyl)-2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropylloxy}-4-hydroxy-N-isobutylbenzamide,

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

 $hydroxypropyl] oxy \} - 4 - [(4 - fluor opiperid in - 1 - yl) carbonyl] phenol, \\$

3-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-[(4,4-difluoropiperidin-1-yl)carbonyl]phenol,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxypropyl)benzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hvdroxvpropyl]oxy}-4-hvdroxv-N-(2-hvdroxv-1,1-dimethylethyl)benzamide.

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-N-cyclopentyl-4-hydroxybenzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxys-N-(2-methoxyethyl)benzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hvdroxypropylloxy}-4-hydroxy-N-(2-hydroxyphenyl)benzamide.

 $2-\{[(2S)-3-(5-\text{chloro-1'}H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl)-2-\\ \text{hydroxypropyl}]\text{oxy}-4-\text{hydroxy-}N-(2-\text{hydroxy-1-methylethyl})\text{benzamide,}$

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 27 of 38

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hvdroxypropylloxy}-4-hvdroxy-N-isobutylbenzamide.

 $2-\{[(2S)-3-(5-\text{chloro-1'}H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl)-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl\}-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl\}-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl\}-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl\}-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl\}-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl\}-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl\}-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl]-1$

hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxyethyl)benzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N-(4-hydroxycyclohexyl)benzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-N-(2,3-dihydroxypropyl)-4-hydroxybenzamide,

Methyl N-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzoyl)serinate,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-N-(1-ethylpropyl)-4-hydroxybenzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-N-(tetrahydrofuran-2-ylmethyl)benzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2hydroxypropylloxy}-4-hydroxy-N-[1-(hydroxymethyl)-2.2-dimethylpropyllbenzamide.

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N-[1-(hydroxymethyl)-2-methylpropyl]benzamide,

 $2-\{[(2S)-3-(5-\text{chloro-1'}H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl)-2-H,3H-\text{spiro}[2-\text{benzofuran-1,4'-piperidin}]-1'-yl\}$

 $hydroxypropyl]oxy\}-4-hydroxy-N-[3-(1-hydroxyethyl)phenyl]benzamide,\\$

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-N-(cyclopropylmethyl)-4-hydroxybenzamide.

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

hydroxypropyl]oxy}-4-hydroxy-N-pyrrolidin-1-ylbenzamide,

N-[(1R,45)-bicyclo[2.2.1]hept-2-yl]-2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxybenzamide,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 28 of 38

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-hydroxy-N-(2-hydroxy-1-phenylethyl)benzamide,

2-{[(2S)-3-(5-chloro-1'H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-hydroxypropylloxy}-4-hydroxy-N-(2-hydroxycyclohexyl)benzamide,

1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-hydroxybenzoyl)pyrrolidine-3-carboxamide trifluoroacetate,

1-(2-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-hydroxybenzoyl)-L-prolinamide trifluoroacetate,

 $2-\text{chloro-}5-\{[(2S)-3-(5-\text{chloro-}1'H,3H-\text{spiro}[1-\text{benzofuran-}2,4'-\text{piperidin}]-1'-yl)-2-\\ \text{hydroxypropyl}]\text{oxy}-4-\{[(3R)-3-(\text{dimethylamino})\text{pyrrolidin-}1-yl]\text{carbonyl}\}\text{phenol}\\ \text{bis(trifluoroacetate)}.$

 $2-chloro-5-\{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy\}-4-\{[(3R)-3-(hydroxymethyl)pyrrolidin-1-yl]carbonyl\}phenol trifluoroacetate, \\$

2-chloro-5-{[(2S)-3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}-4-{[(3S)-3-(hydroxymethyl)pyrrolidin-1-yl]carbonyl}phenol trifluoroacetate,

2-chloro-5-{[(2S)-3-(5-fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropyl]oxy}-4-(pytrolidin-1-ylcarbonyl)phenol trifluoroacetate,

N-(2-[[(2R)-3-(5-Fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropylloxyl-4 methoxyphenyl)acetamide.

Methyl 2-{[(2S)-3-(5-fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropylloxy}benzoate,

2-{[(2S)-3-(5-Fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropylloxy}benzoic acid (hydrochloride),

(3S)-1-(2-{[(2S)-3-(5-Fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hvdroxypropyl]oxy}benzoyl)pyrrolidin-3-ol,

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 29 of 38

3-{[(2S)-3-(5-Fluoro-1'*H*,3*H*-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropylloxy}-4-(pyrrolidin-1-ylcarbonyl)phenol,

N (4-fluoro 2-[[(2S) 3 (5-fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl) 2-hydroxypropylloxy|phenyl)acetamide,

N-{5-chloro-2-{3-(5-chloro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropoxy]-4-hydroxyphonyl}-cyclopentanecarboxamide,
N-{5-chloro-2-{3-(5-fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-

hydroxypropoxy] 4-hydroxyphenyl] cyclopentanecarboxamide,

N-{5-chloro-4-hydroxy-2-{2-hydroxy-3-(I'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)propoxy|phenyl|eyelopentaneearboxamide,

N (5 Chloro 2 [[(2S) 3 (5 chloro 1 H,3H spiro[1 benzofuran 2,4' piperidin] 1' yl) 2hydroxypropyl]exy] 4 hydroxyphenyl)benzamide trifluoroacetate,

N (5 Chloro 2 [[(2S) 3 (5 fluoro 1 H,3H spiro[1 benzofuran 2,4' piperidin] 1' yl) 2hydroxypropyl]cxy] 4 hydroxyphenyl)benzamide trifluoroacetate,

 $\label{eq:Normalized} N (S-Chloro-2-[[(2S)-3-(S-chloro-1^lH,3H-spiro[1-benzofuran-2,4^l-piperidin]-1^l-yl)-2-hydroxypropyl]oxy]-4-hydroxyphenyl)urea-trifluoroacetate,$

N (5 Chloro-2-{[(2S)-3-(5-fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy]-4-hydroxyphenyl)urea-trifluoroacetate;

N (5-chloro 2 [[(25)-3-(5-fluoro-1/H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy] phenyl)urea;

N (5-chloro 2- [[(2S) 3 (5-chloro 1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy}phenyl)urea;

N (2 [[(2S) 3 (5 fluoro 1!H,3H-spiro[1 benzofuran 2,4' piperidin] 1' yl) 2-hydroxypropylloxyl phenyllurea;

 $\label{eq:local_sym} N-(2-[\{(2S)-2-\mbox{hydroxy-3-}(1+H,3H-\mbox{spiro}[1-\mbox{benzofuran-2,4'-piperidin}]-1'-yl)propyl]oxyl-phenyl)urea,$

(II)

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 30 of 38

N-(4-fluoro-2-[[(2S)-3-(5-fluoro-1'H,3H-spiro[1-benzofuran-2,4'-piperidin]-1'-yl)-2hydroxypropylloxy|phenyllurea,

N (4 fluoro 2 - {{(2S)-2-hydroxy-3 - {1!H,3H-spiro[1-benzofuran-2,4!-piperidin}-1!-yl)propyl]oxy]phenyl)urea,

and pharmaceutically acceptable salts of any one thereof.

- (Currently amended) A process for the preparation of a compound of formula (I) or a
 pharmaceutically acceptable salt thereof as defined in claim 1 which comprises,
- (a) reacting a compound of formula

$$X-Y$$
 $(CH_2)_q$
 $(R^2)_n$

wherein m, R¹, n, R², q, X, Y and Z are as defined in claim 1, with a compound of formula

wherein R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , t and R^9 are as defined in claim 1; or

(b) reacting a compound of formula

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 31 of 38

$$(R^1)_m \xrightarrow{X-Y} (CH_2)_q \xrightarrow{R^4} R^6 \xrightarrow{R^6} R^7$$

wherein m, R^1 , n, R^2 , q, X, Y, Z, R^4 , R^5 , R^6 , R^7 and R^8 are as defined in claim 1, with a compound of formula

HO
$$(R^9)_t$$

wherein R^3 , t and R^9 are as defined in claim 1, in the presence of a suitable base; or (e) when R^3 -represents NHC(O) R^{10} , reacting a compound of formula

$$(R^{1})_{m}$$

$$X-Y$$

$$(CH_{2})_{q}$$

$$R^{5}$$

$$R^{8}$$

$$R^{7}$$

$$NH_{2}$$

$$(R^{2})_{n}$$

$$(R^{2})_{n}$$

$$(R^{2})_{n}$$

$$(R^{2})_{n}$$

wherein m, $R^{\frac{1}{7}}$, n, $R^{\frac{2}{7}}$, q, X, Y, Z, $R^{\frac{4}{7}}$, $R^{\frac{5}{7}}$, $R^{\frac{6}{7}}$, $R^{\frac{7}{7}}$, $R^{\frac{8}{7}}$, t and $R^{\frac{9}{9}}$ are as defined in claim 1, with a compound of formula

Applicant : Hossain et al.
Serial No. : 10/520,699
Filed : January 7, 2005
Page : 32 of 38

wherein $L^{\frac{1}{2}}$ represents a leaving group and $R^{\frac{10}{2}}$ is as defined in claim 1; or (d) (c) when R^3 represents $-C(0)NR^{\frac{11}{2}}R^2$, reacting a compound of formula

$$(R^1)_m = Z \xrightarrow{(CH_9)_q} N \xrightarrow{R^4} R^6 \xrightarrow{R^6} C(O)L^2$$

wherein L^2 represents a leaving group and m, R^1 , n, R^2 , q, X, Y, Z, R^4 , R^5 , R^6 , R^7 , R^8 , t and R^9 are as defined in formula (I), with a compound of formula (IX), NHR 11 R 12 , wherein R^{11} and R^{12} are as defined in formula (I); or (e) when R^3 represents NHC(O)R 10 , R^{10} represents NR 14 R 15 and R^{14} and R^{15} both represent hydrogen, reacting a compound of formula (VI) as defined in (e) above with potassium evanate;

and optionally after (a), (b), or (c), (d) or (e) forming a pharmaceutically acceptable salt.

11-12. (Cancelled).

13. (Previously presented) A pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof as claimed in claim 1 in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

Applicant: Hossain et al. Serial No.: 10/520,699 Filed: January 7, 2005 Page: 33 of 38

14. (Currently amended) A process for the preparation of a pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof in association with a pharmaceutically acceptable adjuvant, diluent or carrier which comprises mixing a compound of formula (I)

$$(R^{1})_{m} \xrightarrow{X-Y} (CH_{2})_{q} \xrightarrow{R^{4}} R^{6} \xrightarrow{R^{7}} O \xrightarrow{R^{3}} (R^{9})_{t}$$

wherein

m is 0, 1, 2, 3 or 4;

each R ¹ independently represents halogen, cyano, hydroxyl, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkoxy or sulphonamido;

either X represents a bond, -CH₂-, -O- or -C(O)- and Y represents a bond, -CH₂-, -O- or -C(O)-, or X and Y together represent a group -CH=C(CH₃)- or -C(CH₃)=CH-, and Z represents a bond, -O-, -NH- or -CH₂-, provided that only one of X, Y and Z can represent a bond at any one time and provided that X and Y do not both simultaneously represent -O- or -C(O)-;

n is 0, 1 or 2; each $\ensuremath{R^2}$ independently represents halogen or $C_1\text{-}C_6$ alkyl;

q is 0 or 1; R^3 represents $-NHC(O)R^{10}$, $-C(O)NR^{11}R^{12}$ or $-COOR^{12a}$;

 R^4 , R^5 , R^6 , R^7 and R^8 each independently represent a hydrogen atom or a C_1 - C_6 alkyl group:

t is 0, 1 or 2;

Attorney's Docket No.: 06275-427US1 / 100684-1P US

Applicant: Hossain et al. Serial No.: 10/520.699 Filed : January 7, 2005

: 34 of 38 Page

each R⁹ independently represents halogen, cyano, hydroxyl, carboxyl, C₁-C₆ alkoxy, C1-C6 alkoxycarbonyl, C1-C6 haloalkyl, or C1-C6 alkyl optionally substituted by at least one substituent selected from carboxyl and C1-C6 alkoxycarbonyl;

R +0 -represents a group-C1-C6 alkyl, C2-C6 alkenyl, C3-C6-cycloalkyl, adamantyl, C5-C6-eveloalkenyl, phenyl-or-a saturated or unsaturated 5-to 10-membered heterocyclic ring system comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, each of which may be optionally substituted by one or more substituents independently selected from nitro, hydroxyl, oxo, halogen, carboxyl, C1-C6-alkyl, C1-C6-alkoxy, C1-C6-alkylthio, C1-C6-alkylearbonyl, C1-C6-alkoxycarbonyl, phenyl and NHC(O)-R13, or

R 10 represents a group NR 14 R 15 or O-R 16:

 R^{11} and R^{12} each independently represent (i) a hydrogen atom, (ii) a 3- to 6-membered saturated or unsaturated ring optionally comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur and optionally further comprising a bridging group, the ring being optionally substituted with at least one substituent selected from halogen, hydroxyl, C₁-C₆ alkyl, C1-C6 hydroxyalkyl and C1-C6 haloalkyl,

(iii) a C₁-C₆ alkyl group optionally substituted by at least one substituent selected from halogen. amino, hydroxyl, C1-C6 haloalkyl, carboxyl, C1-C6 alkoxy, C1-C6 alkoxycarbonyl, C1-C6 alkylcarbonylamino and a 3- to 6-membered saturated or unsaturated ring optionally comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur and optionally further comprising a bridging group, the ring being optionally substituted with at least one substituent selected from halogen, hydroxyl, oxo (=O), C1-C6 alkyl, C1-C6 hydroxyalkyl and C1-C6 haloalkyl, or (iv) C1-C6 alkylsulphonyl, or

R¹¹ and R¹² together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring that optionally further comprises a ring nitrogen, oxygen or sulphur atom and that is optionally fused to a benzene ring to form a 8- to 11-membered ring system, the heterocyclic ring or ring system being optionally substituted with at least one substituent selected from halogen, hydroxyl, amido, C1-C6 alkyl, C1-C6 hydroxyalkyl, C1-C6 alkoxy,

Applicant: Hossain et al. Attorney's Docket No.: 06275-427US1/100684-1P US

Serial No.: 10/520,699 Filed: January 7, 2005 Page: 35 of 38

 $\label{eq:c1-C6-alkoxycarbonyl, C1-C6-alkylamino, di-C1-C6-alkylamino, di-C1-C6-alkylamino, di-C1-C6-alkylamino, di-C1-C6-alkylamino, di-C1-C6-alkylamino, di-C1-C6-alkylaminocarbonyl, di-C1-C6-alkylaminocarbonyl, phenyl, phenylcarbonyl, phenylcarbonyl,$

R 12a represents a hydrogen atom or a C1-C6 alkyl group;

R¹³-represents a C₁-C₆-alkyl, amino or phenyl group;

R¹⁴ and R¹⁵ each independently represent a hydrogen atom, or a group C₁-C₆ alkyl, C₁-C₆ alkylsulphonyl, phenyl or a saturated or unsaturated 5- to 10 membered heteroeyelie ring system comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, each group being optionally substituted as defined above for R¹⁰, or

R¹⁴ and R¹⁵ together with the nitrogen atom to which they are attached form a 4-to 7-membered saturated heterocyclic-ring that optionally further comprises a ring nitrogen, oxygen or sulphur atom, the heterocyclic ring being optionally substituted by at least one hydroxyl; and R¹⁶ represents a hydrogen atom, or a group C₁-C₆ alkyl, phenyl-or-a saturated or unsaturated 5- to 10-membered heterocyclic ring system-comprising at least one ring heteroatom

selected from nitrogen, oxygen and sulphur, each group being optionally substituted as defined

or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable adjuvant, diluent or carrier.

15-22. (Cancelled).

above for R 10: